REMARKS

Formal Matters

Claims 1-4 and 6-12 are pending and all are rejected under 35 USC § 103(a). Applicants respectfully traverse and request reconsideration of the application in view of the remarks set forth herein.

Rejection Under 35 USC § 103(a)

1. FERRARINI et al.

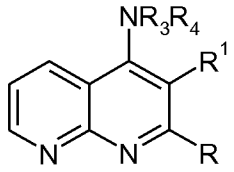
Claims 1-4 and 6-12 are rejected under 35 USC § 103(a) as being obvious solely over FERRARINI et al., FARMACO, 55 (2000), pp. 603-610 ("FERRARINI et al."). Specifically, Examiner asserts that FERRARINI et al. teach 1,8-naphthydines:

> "*which appears to be of the presently claimed compounds covered by formula(I) as in claim 1. See table 2 on page 606 where compounds 2d, 5a, 5b, and 5c where R2 is Cl, R1 is H.*" Office Action, 10/19/2009, p.6.

Applicants respectfully traverse.

Contrary to Examiner's assertion, Applicants respectfully submit that 1,8-naphthydines of FERRARINI et al. are not within the scope of claim 1. Copied below is Applicants' formula (I) of claim 1 along with the Table 2 compounds of FERRARINI et al.

Applicants' claimed compounds:

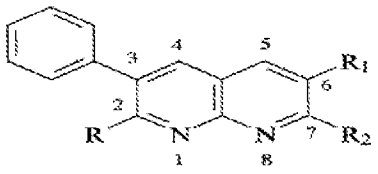


(I)

wherein

R is halo and R^1 is aryl or heteroaryl;

FERRARINI et al. compounds:



Comp.	R	R_1	R_2
2d	Pipz	H	NH_2
3d	Pipz	H	OH
5a	Morph	H	Cl
5b	Pip	H	Cl
5c	Cep	H	Cl

Claim 1 compounds contain a pyridine ring that is completely unsubstituted while FERRARINI et al. Table 2 compounds require substitution on *both* pyridine rings. Three substituent groups (R, R_1, NR_3R_4) are required on the claim 1 compounds. Four substitutions (R, R_1, R_2, phenyl) are required for the FERRARINI et al. compounds. Claim 1 compounds contain an amino group (NR_3R_4) in the *para* position from the nitrogen atom on the pyridine ring. The FERRARINI et al. compounds are *not* substituted at this position. Further, the FERRARINI et al. compounds cannot be simultaneously amino substituted and halo substituted as required in Applicants' claim 1 compounds (*compare* compounds 2d with 5a, 5b, 5c of FERRARINI et al.). Accordingly, the compounds of FERRARINI et al. do not fall within the scope of claim 1.

Examiner further contends that compounds of FERRARINI et al. are "positional isomers" of the claim 1 compounds. Office Action, 10/19/2009, p.6. Applicants respectfully submit they are not. The respective structures do not have "the same molecular formula" as required of positional isomers. The number of substitutions and the substituent groups are not the same as further discussed above.

Examiner further contends that the compounds of FERRARINI et al. are "homologues" of the claim 1 compounds. Office Action, 10/19/2009, p.6. Applicants respectfully submit they are not. Examiner expressly defines homologues as:

> "*Compounds that differ only by the presence of an extra methyl or ethyl group*. . ." Office Action, 10/19/2009, p.6.

The compounds of claim 1 and FERRARINI et al. differ by more than an extra methyl or ethyl group. These compounds are structurally different both in terms of the number of possible substituent groups and the selection of permissible substituents. Accordingly, the respective compounds cannot be considered to be homologues.

Examiner previously agreed in distinguishing these compounds from one another, stating:

> *"Presently claimed compounds differ mainly from BADAWNWH et al. and FERRARINI et al. (IDS references) in having one naphthyridine ring completely unsubstituted wherein the reference it is always occupied by at least one group for example OH."* Office Action, 11/30/2006, p.11.

Examiner provides no basis for this change in position. For completeness of record, Applicants note that the arguments presented above were also previously presented in Applicants' Amendment of July 23, 2008. Examiner has not substantively addressed this change in position nor Applicants' prior remarks in the present office action.

Finally, there is no teaching or suggestion to modify the compounds of FERRARINI et al. to arrive at the compounds of claim 1. The Examiner bears the burden of providing a factual basis or rational as to why one of ordinary skill in the art would have been motivated to modify FERRARINI et al. to arrive at the instantly claimed compounds. Thus, to establish a *prima facie* case of obviousness, the Examiner must show there existed a reason to modify FERRARINI et al. in a manner that would result in the claimed compounds. The Examiner has failed to provide such a factual basis or rationale.

FERRARINI et al. is non-analogous art. The reference teaches compounds possessing human anti-platelet activity, whereas compounds of the present invention possess fungicidal activity. The skilled person would not consider the teaching of anti-platelet activity in FERRARINI et al. to be relevant to the problem of identifying new compounds possessing antifungal activity. Section 707.07(f) of the MPEP reminds that it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). Examiner has made no such showing.

Further, FERRARINI et al. teaches:

> "*However, on the basis of pharmacological results, no structure activity relationship can be deduced."* (Abstract).

This demonstrates that even in the anti-platelet field, the lack of SAR means predictions cannot be made regarding the biological activity of any particular compound possessing the naphthyridine ring system. Applicants submit that the lack of such predictive ability extends to compounds possessing antifungal activity as well. FERRARINI et al. provides no teaching, suggestion or motivation to prepare the compounds of the present invention.

Thus, Examiner has failed to meet the *prima facie* burden. Applicants respectfully request that Examiner withdrawal the rejection of claims 1-4 and 6-12 under 35 USC § 103(a) in view of FERRARINI et al.

2. BADAWNEH et al.

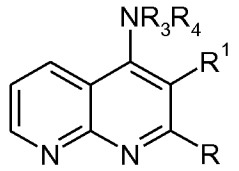
Claims 1-4 and 6-12 are rejected under 35 USC § 103(a) as being obvious solely over BADAWNEH et al., FARMCO, 57 (2002), pp. 631-639 ("BADAWNEH et al."). Specifically, Examiner asserts that the:

> "[p]resently claimed compounds differ from the [BADAWNEH et al. compounds] in containing H at wherein prior art teaches a methyl group… See Table 1, compounds 6 and 8 on page 633". Office Action, 10/19/2009, p.8.

Applicants respectfully traverse.

Multiple differences exist between these respective compounds. Copied below is Applicants' formula (I) of claim 1 along with the Table 1 compounds of BADAWNEH et al.

Applicants' claimed compounds:



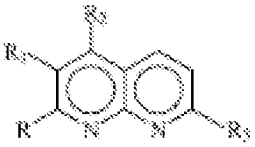
(I)

wherein

R is halo and R^1 is aryl or heteroaryl;

BADAWNEH et al. compounds:

Table 1
Physical data of 1,8-napthyridine derivatives



Comp.	R	R_1	R_2	R_3
1	OH	CH_3	OH	CH_3
2	OH	$C_6H_5CH_2$	OH	CH_3
3	Cl	CH_3	Cl	CH_3
4	Cl	$C_6H_5CH_2$	Cl	CH_3
5	Morph	CH_3	Cl	CH_3
6	Morph	$C_6H_5CH_2$	Cl	CH_3
7	Pip	CH_3	Cl	CH_3
8	Pip	$C_6H_5CH_2$	Cl	CH_3

Claim 1 compounds contain a pyridine ring that is completely unsubstituted while BADAWNEH et al. Table 1 compounds require substitution on *both* pyridine rings. Three substituent groups (R, R_1, NR_3R_4) are required on the claim 1 compounds. Four substitutions (R, R_1, R_2, R_3) are required for the BADAWNEH et al. compounds. The BADAWNEH et al. compounds are not amino substituted. Claim 1 compounds contain an amino group (NR_3R_4) in the *para* position from the nitrogen atom on the pyridine ring. The BADAWNEH et al. compounds contain a halo at the *para* position. Further, R_1 of claim 1 compounds is aryl or heteroaryl. Corresponding R_1 of BADAWNEH et al. is benzyl. Accordingly, the compounds of BADAWNEH et al. contain significant differences from compounds of claim 1.

Examiner further contends that the compounds of BADAWNEH et al. are "homologues" of the claim 1 compounds. Office Action, 10/19/2009, p.8. Applicants respectfully submit they are not. Examiner expressly defines homologues as

> "*Compounds that differ only by the presence of an extra methyl or ethyl group. . . Office Action*." 10/19/2009, p.8.

The compounds of claim 1 and BADAWNEH et al. differ by more than an extra methyl or ethyl group. These compounds are structurally different both in terms of the number of possible substituent groups and the selection of permissible substituents as described above. Accordingly, the respective compounds cannot be considered to be homologues.

Examiner previously agreed in distinguishing these compounds from one another, stating:

> "*Presently claimed compounds differ mainly from BADAWNWH et al. and FERRARINI et al. (IDS references) in having one naphthyridine ring completely unsubstituted wherein the reference it is always occupied by at least one group for example OH*." Office Action, 11/30/2006, p.11.

Finally, there is no teaching or suggestion to modify the compounds of BADAWNEH et al. to arrive at the compounds of claim 1. The Examiner bears the burden of providing a factual basis or rational as to why one of ordinary skill in the art would have been motivated to modify BADAWNEH et al. to arrive at the instantly claimed compounds. Thus, to establish a *prima facie* case of obviousness, the Examiner must show there existed a reason to modify BADAWNEH et al. in a manner that would result in the claimed compounds. The Examiner has failed to provide such a factual basis or rationale.

BADAWNEH et al. is non-analogous art. The reference teaches compounds possessing human anti-tubercular (e.g., tuberculosis) activity, whereas the compounds of the present invention possess fungicidal activity. The skilled person would not consider the teaching of anti-tubercular activity in BADAWNEH et al. to be relevant to the problem of identifying new compounds possessing antifungal activity. Section 707.07(f) of the MPEP reminds that it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). Examiner has made no such showing.

Thus, Examiner has failed to meet the *prima facie* burden. Applicants respectfully request that Examiner withdrawal the rejection of claims 1-4 and 6-12 under 35 USC § 103(a) in view of BADAWNEH et al.

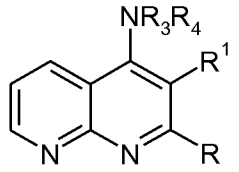
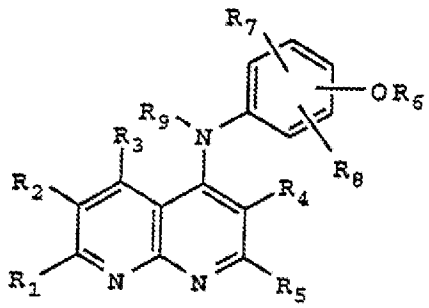
3. ARMITAGE et al. & COLLINS et al.

Claims 1-4 and 6-12 are rejected under 35 USC § 103(a) as being obvious over ARMITAGE et al., WO93/13097 ("ARMITAGE et al.") and COLLINS et al., WO92/07468 ("COLLINS et al."). Specifically, Examiner asserts that:

> "*Both references teach naphthyridine derivatives which embraces [sic] presently claimed invention. See entire documents especially formula (I) in abstract, and on page 2, examples and claims in ARMITAGE. See abstract and compounds of formula (I), examples and claims in COLLINS.*
>
> *Instant claims differ from the reference in that they are of different generic scope. Office Action*." 10/19/2009, p.9.

Applicants respectfully traverse.

Neither ARMITAGE et al. nor COLLINS et al. disclose compounds which "embrace" or "generically disclose" the presently claimed compounds. Copied below is Applicants' formula (I) of claim 1 along with formula (I) compounds from ARMITAGE et al.

Applicants' claimed compounds:	**ARMITAGE et al. compounds:**
 (I) wherein R is halo and R^1 is aryl or heteroaryl;	 (I)

Claim 1 compounds contain an amino group (NR_3R_4) in the *para* position from the nitrogen atom on the pyridine ring. No amino substitution is permitted on the naphthyridine ring of ARMITAGE et al.

The corresponding position of ARMITAGE et al. requires aniline substitution only, which is not encompassed by presently claimed compounds, e.g., neither R_3 nor R_4 are independently phenyl. Claim 1 compounds require aryl or heteroaryl at R_1. ARMITAGE et al. does not disclose aryl or heteroaryl groups in the corresponding position at R_4. Accordingly, the claimed compounds are not within the "generic scope" of ARMITAGE et al.

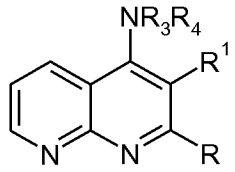
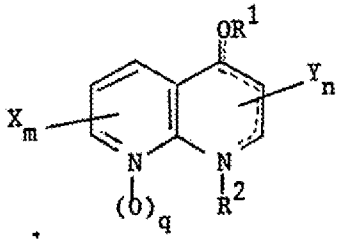
There is no teaching or suggestion to modify the compounds of ARMITAGE et al. to arrive at the compounds of claim 1. The Examiner bears the burden of providing a factual basis or rational as to why one of ordinary skill in the art would have been motivated to modify ARMITAGE et al. to arrive at the instantly claimed compounds. Thus, to establish a *prima facie* case of obviousness, the Examiner must show there existed a reason to modify ARMITAGE et al. in a manner that would result in the claimed compounds. The Examiner has failed to provide such a factual basis or rationale.

ARMITAGE et al. is non-analogous art. The reference teaches compounds possessing anti-rheumatic (e.g., rheumatoid arthritis) activity, whereas the compounds of the present invention possess fungicidal activity. The skilled person would not consider the teaching of anti-rheumatic in ARMITAGE et al. to be relevant to the problem of identifying new compounds possessing antifungal activity. Section 707.07(f) of the MPEP reminds that it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). Examiner has made no such showing.

ARMITAGE et al. does not support Examiner's assertion of obviousness, either alone or in combination with COLLINS et al. Accordingly, ARMITAGE et al. may not be combined with COLLINS et al. in support of the present obviousness rejection. No further discussion is necessary as Examiner does not assert that the presently claimed invention is obvious over COLLINS et al.

alone. Nevertheless, in order to further advance the prosecution, Applicants address COLLINS et al. below.

Copied below is Applicants' formula (I) of claim 1 along with formula (I) compounds from COLLINS et al.

Applicants' claimed compounds:	**COLLINS et al. compounds:**
 (I) wherein R is halo and R^1 is aryl or heteroaryl;	 (I)

COLLINS et al. is limited to naphthyridines possessing an oxygen substituent, either oxo, hydroxyl or an acetoxy group, in the *para* position on the ring. Compounds of the claimed invention do not possess such oxygen substituents. COLLINS et al. teach substitution from the nitrogen atoms of naphthyridines. Claim 1 compounds are not substituted on the nitrogen atom. Further, claim 1 compounds contain di-substitution on the carbon atoms within the pyridine ring whereas COLLINS et al. teach only corresponding and optional mono-substitution. Claim 1 compounds contain an amino group (NR_3R_4) in the *para* position from the nitrogen atom on the pyridine ring whereas COLLINS et al. do no teach amino substitution in the corresponding position.

Finally, there is no teaching or suggestion to modify the compounds of COLLINS et al. to arrive at the compounds of claim 1. The Examiner bears the burden of providing a factual basis or rational as to why one of ordinary skill in the art would have been motivated to modify COLLINS et al. to arrive at the instantly claimed compounds. Thus, to establish a *prima facie* case of obviousness, the Examiner must show there existed a reason to modify COLLINS et al. in a manner that would result in the claimed compounds. The Examiner has failed to provide such a factual basis for rationale.

COLLINS et al. is non-analogous art. The reference teaches compounds possessing herbicidal activity, whereas the compounds of the present invention possess fungicidal activity. The skilled person would not consider the teaching of herbicidal activity in COLLINS et al. to be relevant to the problem of identifying new compounds possessing antifungal activity. Section 707.07(f) of the MPEP reminds that it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). Examiner has made no such showing.

Neither ARMITAGE et al. nor COLLINS et al. disclose compounds which generically disclose the presently claimed compounds, nor are these references considered relevant to teachings of compounds with antifungal activity. Applicants respectfully request that Examiner withdrawal the rejection of claims 1-4 and 6-12 under 35 USC § 103(a) based on ARMITAGE et al. and COLLINS et al.

Respectfully submitted,

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